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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/770,294	02/02/2004	Andrew D. Miller	YOUZ 2 00059-2	1414

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EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
07/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/770,294	MILLER ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-75* is/are pending in the application.

4a) Of the above claim(s) *71-75* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

1. This action is response to Applicant's remarks filed May 16, 2007. Claims 1-22 have been cancelled. Claims 71-75 have been withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Applicant's submission of Carmona et al submitted May 16, 2007 is acknowledged.

Rejection Maintained

2. The rejection under 35 U.S.C. 112, first paragraph is maintained for claims 23-70 for the reasons set forth on pages 3-6, paragraph 4 of the Final Office Action.

The rejection is reiterated below:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23-70 are directed to a method for treating a genetic disorder or condition or disease in a patient in need of treatment comprising administering an effective amount of a compound comprising a cholesterol group or derivative thereof having linked thereto a head group, wherein the head group is more positive than the head group of DC-Chol; further wherein the head group is a straight chain polyamine; further wherein two or more of the amine groups of the polyamine are separated by an ethylene group.

The claims broadly encompasses gene therapy, wherein the claimed method of treating a genetic disorder or condition or disease, is treated by administering a cationic lipid compound admixed with or associated with a nucleotide sequence.

The specification teaches that the compound of the invention is used in gene therapy, especially gene transfer (page 1). The specification teaches that one aspect of gene therapy involves the introduction of foreign nucleic acid into cells so that it is expressed protein may carry out a desired therapeutic function (page 1). The specification teaches that this type of therapy includes the insertion of TK, TSG or ILG gene to treat cancer, the insertion of the CFTR gene to treat cystic fibrosis, the insertion of the NGF, TH or LDL genes to treat neurodegenerative and cardiovascular disorders, the insertion of the IL-1 antagonist gene to treat rheumatoid arthritis, the insertion of the HIV antigens and the TK genes to treat AIDS and CMV infections, the insertion of antigens and cytokines to act as vaccines and the insertion of β-globin to treat haemoglobinopathic conditions such as thalassaemias (page 1). There are no working examples in the instant specification to guide the skilled artisan in practicing the claimed method.

The state of the art for gene therapy as discussed by Vile et al *(Gene Therapy,*
Vol. 7, pp. 2-8, 2000) is unpredictable. Vile et al teach that the problems in which gene therapy for cancer will take into the next millennium focus far less on the choice of therapeutic gene(s) to be used than on the means of delivering them. Vile et al teach that there is already a battery of genes that we know are very effective in killing cells and if these genes can be expressed at the right site and at appropriate levels therapy may be occur (page 2). However, until the perfect vector is developed, the choice of gene will remain crucially important in order to compensate for the deficiencies of the vectors we currently have available (page 2, 1st paragraph, left column). Vile et al teach that whatever its mechanism, no single genes can be a serious contender unless it has a demonstrable bystander effect (page 2, right column) and the requirement for such a bystander effect stems directly from the poor delivery efficiency provided by current vectors (page 2, right column). Vile et al teach that a genuine ability to target delivery systems to tumor cells distributed widely throughout the body of a patient would simultaneously increase real titers and efficacy. Vile et al teach that in truth, no such systemically targeted vectors exist yet. Vile et al teach that injection of vectors into the bloodstream for the treatment of cancer requires not only that the vectors be targeted (to infect only tumor cells) but also that they by protected (from degradation, sequestration or immune attack) for long periods of time so that they can reach the appropriate sites for infection. Moreover, having reached such sites, the vectors must be able to penetrate into the tumor from the bloodstream before carrying out their targeted infection (page 4, bottom left column and top right column). In addition, Rochlitz C. F. *(Swiss Medicine Weekly, 131:4-9, 2001)* teaches that none of the more than one hundred clinical studies performed so far had formally proven efficacy of the approach (gene therapy) in any human disease. Rochilitz teaches that although anecdotal reports of tumor responses are becoming more frequent in several human malignancies, the situation has not changed dramatically." (see page 8, bottom of page). Rochlitz teaches that the main problems are still the lack of vectors with high

transduction efficiency *in vivo*, the low tumor specificity of available systems, and our incomplete knowledge of molecular tumor pathology" (pages 8-9).

Thus, as taught above the state of the art regarding gene therapy is considered highly unpredictable. Furthermore, it would take one skilled in the art an undue amount of experimentation to determine what route of administration (e.g. intravenous, dermal,
nasal, rectal, vaginal, inhalation, or topical administration) would result in a therapeutic response using a recombinant virus, lentivirus, adenovirus, retrovirus or bacterium comprising the nucleic acid encoding the antigen. The state of the art regarding the route of administration for gene therapy as exemplified by Verma et al, (*Nature, Vol. 389, No. 6648, pages 239-242, 1997)*, indicates that factors including the nature of the diseases and/or disorders, the nature of a DNA and/or target tissue, and a delivery system and/or amounts of the DNA complexes employed in the delivery system that would generate a therapeutic effect *in vivo* must be considered for any gene therapy method to be successful (page 238, columns 1 and 2). Therefore, the skilled artisan at the time the invention was made recognized the lack of predictability of the nature of the art and state of the prior art to which the instant invention pertains. .Also, such disclosures clearly indicate that the amount of direction or guidance presented in the specification is limited, and would not permit a person skilled in the art to use the invention without undue experimentation at the time the invention was made.

In view of the lack of predictability of the art to which the invention pertains, the lack of established clinical protocols for effective gene therapies, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for treating a genetic disorder, or condition or disease in a patient.

Applicant's Arguments

Applicant urges that they have submitted Carmona et al that discloses a method for treating a disease, namely hepatitis B virus by administering an effective amount of compound according to the claimed invention namely *N*1-cholesteryloxycabonyl-3,7-diazononane-1,9-diamine (CDAN). Applicant urges that in view of the specification, the state of the art and the submission of

Carmona et al, this evidence enables one skilled in the art to practice the claimed invention.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed May 16, 2007 have been fully considered but they are not persuasive.

It is the Examiner's position that the specification is not enabled for the claimed method. The claims encompass treating *any and all* genetic disorders, *any and all* conditions and *any and all* diseases. The Carmona et al teach the *treatment of one condition* (hepatitis B virus) within the broadly claimed genus of genetic diseases, conditions and disorders encompassed by the claims. It should be remembered that the claimed invention encompasses for example, diseases such as HIV, malaria, Huntington's disease, all forms of cancer to name a few. Thus, Carmona et al do not provide evidence to enable the *broad* genus of genetic disorder, conditions or diseases that are encompassed by the claimed invention. It should be noted that hepatitis B is a disease, however, hepatitis B is not a genetic disorder or condition which also encompassed by the claimed invention. It should be remembered as pointed out in the rejection above, the state of the art teaches that gene therapy is highly unpredictable. One skill in the art would not reasonably conclude that a compound encompassed by the claimed invention that is used to treat *one specific disease* (hepatitis B virus) can be used treat the broad genus of *any and all* genetic

disorders or *any and all* diseases or *any and all* conditions that are encompass by the claims.

In view of the lack of predictability of the art to which the invention pertains, the lack of established clinical protocols for effective gene therapies, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for treating *any and all* genetic disorder, or *any and all* conditions or any *and all* disease in a patient.

It appears that Carmona et al is a manuscript that has been submitted to a peer review journal. It should be noted that Carmona et al insufficient to overcome the present rejection.

In view of all of the above, the rejection under 112, first paragraph is maintained.

Status of Claims

3. No claims allowed.

Conclusion

4. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (571) 273-8300.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday –Thursday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Jeffery Siew can be reached at (571) 272-0787.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov./>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vanessa L. Ford
Biotechnology Patent Examiner
July 16, 2007

NITA MINNIFIELD
PRIMARY EXAMINER